

**Title: Synthesis and *in vitro* evaluation of pyridinium type acetylcholinesterase inhibitors**

Author: Anna Kopečková

Nerve agents are extremely toxic substances. As prophylactics against these compounds, reversible acetylcholinesterase (AChE) inhibitors are used in the Czech Army. The goal of the thesis was to synthesise new potential inhibitors and evaluate their *in vitro* inhibition activity.

The compounds were designed as asymmetrical bisquaternary molecules. Their structure was derived from isochinoline and 4-benzylpyridine; these two molecules were connected with variable connecting linkages (5–12 carbons).

The synthesis involved two steps. Reactions of both steps took place in acetonitrile at 70 °C. Afterwards, the compounds were purified and their identity was confirmed with NMR-analysis, mass spectrometry and elementary analysis. The Ellman's method was used for the inhibitory potential evaluation.

Eight compounds were successfully prepared. All of them showed promising inhibitory potential ( $IC_{50}$  values  $10^{-7}$ – $10^{-8}$  mol/l). The strongest inhibitors were compounds bearing heptylenic and decylenic connecting linkage ( $IC_{50}$  0,05  $\mu$ M). The selectivity towards AChE decreased with prolonging connecting linkage.